CHAPTER 4

Development of a Scalable Route for the Synthesis of Imidazo[1,2-a]pyridines under Metal and Solvent Free Conditions

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4.1 Introduction

In the past decade, tremendous efforts have been made towards the synthesis of bioactive heterocyclic molecules and natural products through direct C–C, C–N, C–S and C–O etc. bonds construction by C–H bond functionalization (Pericherla et al. 2013, Chen et al. 2009, Dangel et al. 2002). Nitrogen containing bridgehead heterocyclic compounds like imidazo[1,2-a]pyridines and imidazo[2,1-b]thiazoles are the most imperative class of naturally occurring as well as synthetic compounds with several activities, present in numerous drugs and organic functional materials (Bhagat et al. 2017, Rupert et al. 2003). Out of these compounds, imidazo[1,2-a]pyridines have been extensively studied, presenting a remarkable spectrum of major biological activities such as antipyretic (Almirante et al. 1965), antiviral (Elhakmaoui et al. 1994), antiulcer (Starrett et al. 1989), anticancer (Hamdouchi et al. 1999), antibacterial (Byth et al. 2004) and anti-inflammatory (Lacerda et al. 2009) properties. It also function as nonpeptide B_2 receptor antagonists (Abe et al. 1998), GABA and benzodiazepine receptor agonists (Humphries et al. 2006). These heterocycles are also present in clinical important medicines such as anti-HIV drug (GSK812397) (Boggs et al. 2009), alpidem (Jain et al. 2004), olprinone (Mizushige et al.

2002), zolpidem (Humphries et al. 2006) and zolimidine (Almirante et al. 1965) (**Figure 4.1**).

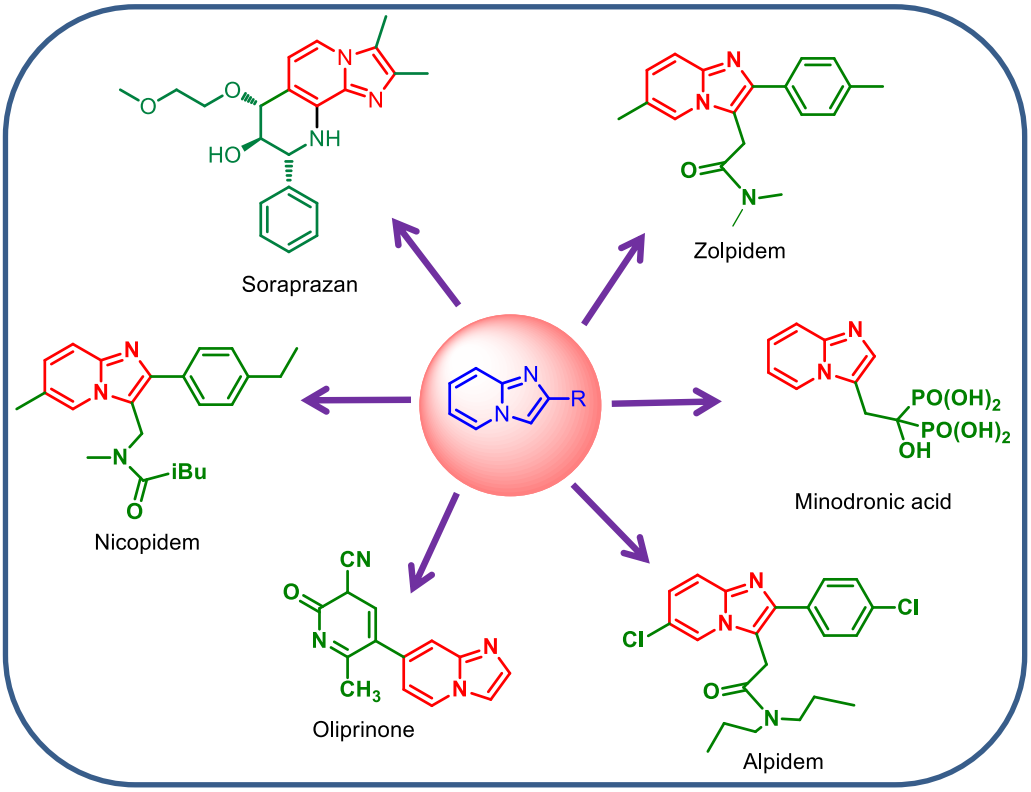


Figure 4.1: Drugs containing imidazo[1,2-a]pyridines moiety.

The usefulness of imidazo[1,2-a]pyridines has provoked great interest in the development of efficient methodologies to synthesize these bicyclic ring systems. Therefore, numerous methods have been established for the synthesis of imidazo[1,2-a]pyridines scaffold by the reaction of 2-aminopyridine with numerous substrates such as methyl aryl ketone (Meng et al. 2015), α-halo ketones (Zhu et al. 2009), alkynes derivatives (He et al. 2012) etc. These reactions generally perform in the presence of Lewis

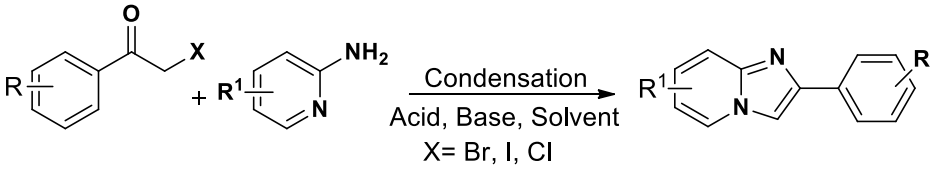
acid (Ge et al. 2013) or metal catalyst Cu (Cao et al. 2012, Pericherla et al. 2013), Fe (Santra et al. 2013), Zn (Liu et al. 2011), Ag (He et al. 2012) (**Scheme 4.1 A**). Stasyuk reported iodine mediated synthesis of imidazo[1,2-a]pyridine by the reaction of 2-aminopyridine and aryl methyl ketones in the presence of base (Stasyuk et al. 2012). Synthesis of imidazo[1,2-a]pyridine have been reported by multicomponent reaction of 2-aminopyridines, isonitriles and aldehydes also known as Groebke-Blackburn- Bienayme reaction (Palani et al. 2012, Masquelin et al. 2006, Khan et al. 2012, Chernyak et al. 2010, Lyon et al. 2004). These approaches are appropriate for a variety of substrates but have few shortcomings such as the use of metal catalyst, use of acid/base, low yield and tedious workup procedure.

Therefore, finding an eco-friendly, simple and practical approach for the synthesis of this important, pharmaceutically active scaffold from the readily available simple precursors is of great interest. Hence in the continuation of existing methods, we have developed a simple method for the synthesis of imidazo[1,2-a]pyridine by the C–H bond activation of methyl ketones, followed by the reaction with appropriate nucleophiles in the presence of KI/TBHP oxidative system under grinding condition (**Scheme 4.1, B**).

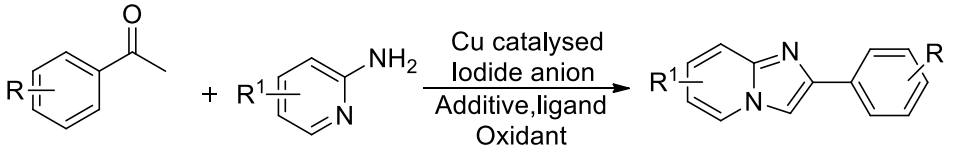
Potassium iodide is less toxic, cheaper and environment friendly as compared to molecular iodine. TBHP has attracted much attention because of their commercial availability inexpensive, easy handling, medium volatility and good solubility in common

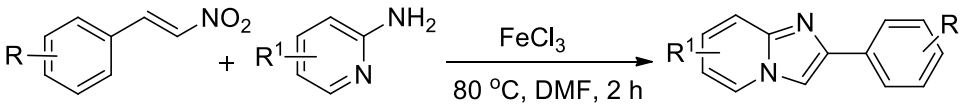
Previous Methods: A

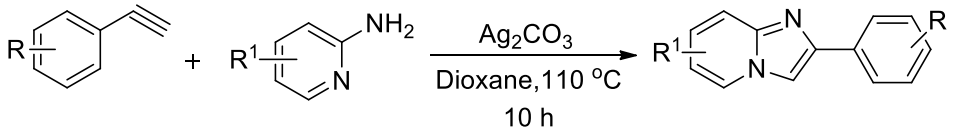
Traditional Method



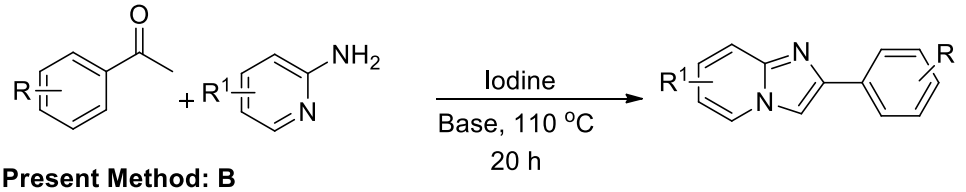
Metal catalysed synthesis:



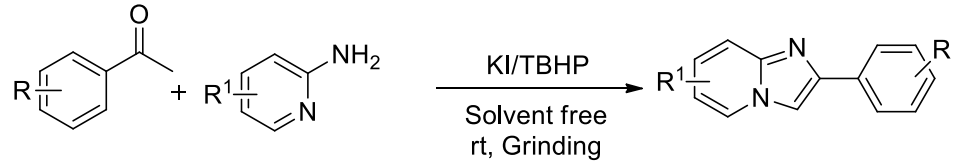




Metal free synthesis by using base:



Present Method: B



Scheme 4.1: Different approach for the synthesis of imidazo[1,2-a]pyridine.

solvents. The most important characteristic of this system (KI/TBHP) is that it has no metal and *tert*-butyl alcohol or water is the only by-product generated by this oxidant (Huang et al. 2014).This efficient catalytic system has attracted numerous chemists to synthesize many important compounds such as N-nitrosamines (Zhang et al. 2013), sulfonated oxindoles (Li et al. 2013), pyrrolo[2,1-a]isoquinolines (Huang et al. 2014), iodophenols (Reddy et al. 2010), polysubstituted furans (Li et al. 2016) and 2-aryl-2-oxazolines (Maheswari et al. 2014). In this context, here we report a simple and efficient KI/TBHP mediated synthesis of imidazo[1,2-a]pyridines from acetophenone derivatives and 2-amino pyridine derivatives for the first time.

Sustainable chemistry has become an important tool in the field of synthetic organic chemistry which comprises the synthesis of organic compounds in the absence of volatile organic solvent (VOCs) or in the solvent free condition. The avoidance of solvents in organic synthesis has become a major concern. Solvent-free, in solid state one-pot synthesis is effective toward organic conversion avoiding harmful volatile organic solvents (VOCs). Benefits associated without solvent or solid state synthesis are such as better worker's safety as well as favorable economics reaction conditions. Grindstone chemistry became an important tool in synthetic organic chemistry which reduces electrical energy consumption. The reactions under grinding are performed without solvent. In grinding methods, reaction starts with the transfer of the very small amount of mechanical energy which is generated

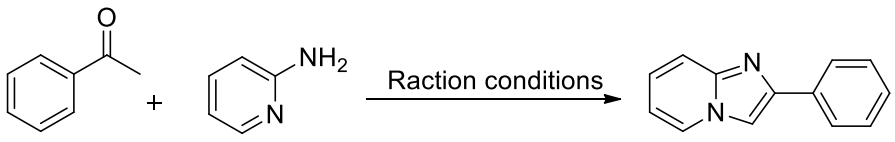
by grinding the reactants in a mortar and pestle and leads to the formation of the product. This solvent-free mechanically stimulated reaction helps in dropping the toxic waste by-products produced and therefore, becomes less damaging to the environment. Hence, we have chosen this technique because it is comparatively superior than existing methods since it has several advantages in terms of environmental impact, effectiveness, requires no special apparatus, cost of solvents & energy sources and easiness of the reaction protocol (Ando et al. 2011, Bose et al. 2004, Friscic et al. 2009, Yu et al. 2019, Nada et al. 2019, Wanyi et al. 2019).

4.2 Result and Discussion

Acetophenone (**1a**) and 2-aminopyridine (**2a**) was chosen as a model substrate with KI/TBHP for optimization of reaction conditions. The consequence of different parameters including solvents, reaction temperature, catalyst loading and reaction time was studied. The reaction performed in the presence of different polar (ethanol, methanol, water, DMSO, chloroform, 1,4-dioxane, THF) and non-polar solvents (toluene, benzene, xylene, hexane) under the stirring condition at room temperature and the results show that the reaction goes only in case of polar solvents with low yield. Out of all polar solvents, ethanol found the good in terms of product yield. In the case of non-polar solvents, no reaction occurs (**Table 4.1, entries 1-12**). Then to increase the product yield we turned our attention to the solvent-free condition at room temperature and the result shows that it gave

the 65% yield in 1h (**Table 4.1, entry 13**). After that the effect of temperature had been tested. By increasing temperature up to 80 ^{o}C under the stirring condition there is no considerable change in the product yield (**Table 4.1, entries 14, 15**). Grindstone chemistry that is useful for the synthesis of different compounds is considered as a green technique. Having this aspect in mind, reaction was performed under the grinding condition for a period in the presence of KI/TBHP. At first we have performed reaction for 5 min, gave the yield of 70% (**Table 4.1, entry 16**) and by increasing time to 8 min gave the yield of 80% (**Table 4.1, entry 17**). Surprisingly, we got the best result with 95% yield of product in 10 min (**Table 4.1, entry 18**). Further, on increasing time up to 15 min there is no considerable change in product yield (**Table 4.1, entry 19**). Further we optimized the amount of the catalyst and oxidant. We have started optimization of catalyst KI with 1 equiv. of TBHP, without KI no product was obtained (**Table 4.1, entry 20**). Next we increase the amount of KI by 0.2 equiv. we got 75% yield (**Table 4.1, entry 21**) of the product in 10 min. By increasing the amount of KI to 0.5 equiv. we got 95% yield in 10 min (**Table 4.1, entry 18**).

Table 4.1: Optimization of reaction condition for imidazo[1,2-a]pyridine[a]



1a **2a** **3aa**

Entry	Solvent	Catalyst/TBHP (Equiv.)	Reaction condition	Time (Min)	Yield[b] (%)
1	Ethanol	KI (0.5)/ 1	Stirring / rt	60	50
2	Methanol	KI (0.5)/ 1	Stirring / rt	60	50
3	Water	KI (0.5)/ 1	Stirring / rt	60	40
4	DMSO	KI (0.5)/ 1	Stirring / rt	60	20
5	1,4Dioxane	KI (0.5)/ 1	Stirring / rt	60	20
6	THF	KI (0.5)/ 1	Stirring / rt	60	15
7	Chloroform	KI (0.5)/ 1	Stirring / rt	60	10
8	DCM	KI (0.5)/ 1	Stirring / rt	60	12
9	Toluene	KI (0.5)/ 1	Stirring / rt	60	No reaction
10	Xylene	KI (0.5)/ 1	Stirring / rt	60	No reaction
11	Hexane	KI (0.5)/ 1	Stirring / rt	60	No reaction
12	Benzene	KI (0.5)/ 1	Stirring / rt	60	No reaction
13	Solvent free	KI (0.5)/ 1	Stirring/rt	60	65
14	Solvent free	KI (0.5)/ 1	50 ^{o}C	60	70
15	Solvent free	KI (0.5)/ 1	80 ^{o}C	60	70
16	Solvent free	KI (0.5)/ 1	Grinding/rt	5	70
17	Solvent free	KI (0.5)/ 1	Grinding/ rt	8	80
18	**Solvent free**	KI (0.5)/ 1	**Grinding/** rt	**10**	**95**
19	Solvent free	KI (0.5)/ 1	Grinding/ rt	15	96
20	Solvent free	KI (0.0)/1	Grinding/ rt	15	No reaction
21	Solvent free	KI (0.2)/1	Grinding/ rt	10	75
22	Solvent free	KI (1.0)/1	Grinding/ rt	15	95
23	Solvent free	KI (0.5)/0	Grinding/ rt	15	No reaction
24	Solvent free	KI (0.5)/ 2	Grinding/ rt	15	95
25	Solvent free	I_2 (0.5) /1	Grinding/ rt	25	80

[a] **Reaction Condition:** Acetophenone (1.0 mmol), 2-aminopyridine (1.2 mmol), KI and oxidant(TBHP)
[b] Isolated yield.

Further any increment in the amount of KI did not make any difference in the yield of the product (**Table 4.1, entry 22**). Next the amount of the oxidant TBHP was optimized with 0.5 equiv. of KI. First we performed reaction in the absence of TBHP no product was obtained (**Table 4.1, entry 23**) and the best result was obtained when the reaction performed with 1 equiv. of TBHP (**Table 4.1, entry 18**). Further any increment in the amount of TBHP did not affect the yield of product (**Table 4.1, entry 24**). These results show that the product was obtained only when the reaction was performed with the KI/TBHP catalytic system. We also performed reaction in the presence of iodine with TBHP and we got the 80% yield in 25 min (**Table 4.1, entry 25**). The results indicate that KI/TBHP found the best catalyst in the grinding protocol.

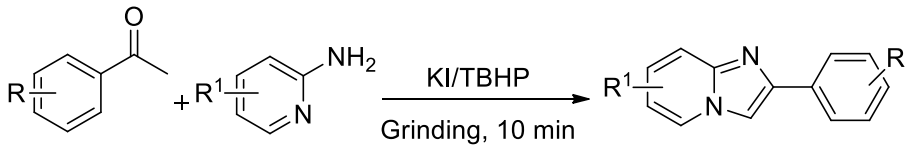
The results indicate that aryl methyl ketone (1.0 mmol), 2-amino pyridine (1.2 mmol) in the presence of KI/TBHP (0.5/1 equiv.) catalytic system under grinding was the optimum condition for the synthesis of imidazo[1,2-a]pyridine. Formation of model compound **3aa** is confirmed by the ^{1}H & ^{13}C NMR spectroscopy (**Figure 4.2 and 4.3**).

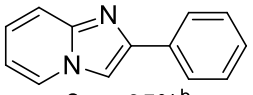
After optimization of reaction condition, the substrate scope has been examined for this transformation. Acetophenones with both the electron donating (methyl, methoxy) and electron withdrawing groups (nitro, fluoro, chloro, bromo) underwent the reation smoothly to give the desired products *viz.* 2-(p-tolyl)imidazo[1,2-a]pyridine (**3ba**), 2-(4-methoxyphenyl)imidazo [1,2-a]pyridine (**3ca**), 2-(3-nitrophenyl)imidazo[1,2-a]pyridine

(**3da**), 2-(4-chlorophenyl) imidazo[1,2-a]pyridine (**3ea**), 2-(4-bromophenyl)imidazo[1,2-a]pyridine (**3fa**), 2-(4-fluorophenyl)imidazo[1,2-a]pyridine (**3ga**) in good to excellent 90-95% yields (**Table 4.2**). 2-(Imidazo[1,2-a]pyridin-2-yl)phenol (**3ha**) which shows effectual excited state intramolecular proton transfer luminescence in the solid state was also fruitfully achieved under optimized reaction conditions with the yield of 89% (**Table 4.2**). It is worth mentioning that 2-(naphthalen-1-yl)imidazo[1,2-a]pyridine (**3la**) was obtained in good yield (**Table 4.2**). Further, to find the generality of the reaction, different heteroatom containing methyl ketones like 2-acetyl pyridine/2-acetyl thiophene were also explored and gave smoothly the corresponding products *viz.* 2-(pyridin-2-yl)imidazo[1,2-a]pyridine (**3ja**), 2-(thiophen-2-yl)imidazo[1,2-a]pyridine (**3ka**) in good yields (**Table 4.2**).

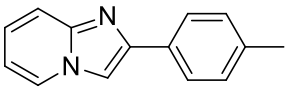
Having explored the scope of different acetophenones next we moved to investigate the scope of nucleophile *i.e.* 2-aminopyridine. To our satisfaction when alkyl and halogen substituted 2-aminopyridines were subjected to this reaction, gave the analogous products *viz.* 8-methyl-2-phenylimidazo[1,2-a]pyridine (**3ab**), 2-(4-methoxyphenyl)-8-methylimidazo[1,2-a]pyridine(**3cb**), 8-methyl-2-(3-nitrophenyl)imidazo[1,2-a]pyridine (**3db**), 2-(4-chlorophenyl)-8-methylimidazo[1,2-a]pyridine (**3eb**), 2-(4-bromophenyl)-8-methylimidazo[1,2-a]pyridine (**3fb**), 2-(4-fluorophenyl)-8-methylimidazo[1,2-a]pyridine (**3gb**), 2-(8-methylimidazo[1,2-a]pyridin-2-yl)phenol(**3hb**), 4-(8-methylimidazo[1,2-a]pyridin-2-yl)phenol (**3ib**),

Table 4.2: Substrate scope[a]

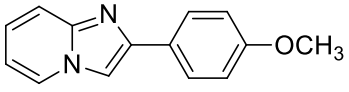




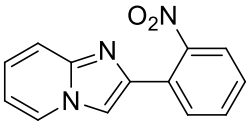
3aa: 95%[b]



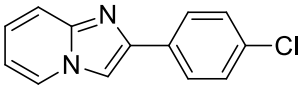
3ba: 93%



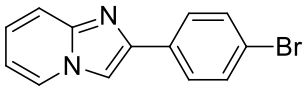
3ca: 94%



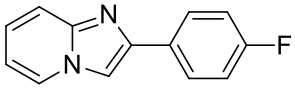
3da: 95%



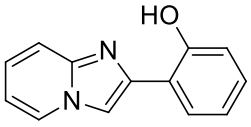
3ea: 92%



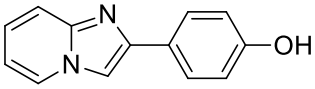
3fa: 90%



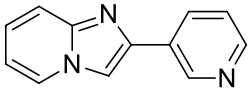
3ga: 94%



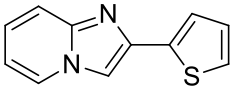
3ha: 89%



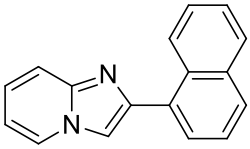
3ia: 88%



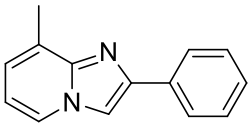
3ja: 85%



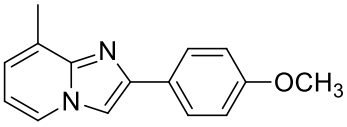
3ka: 92%



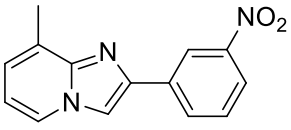
3la: 93%



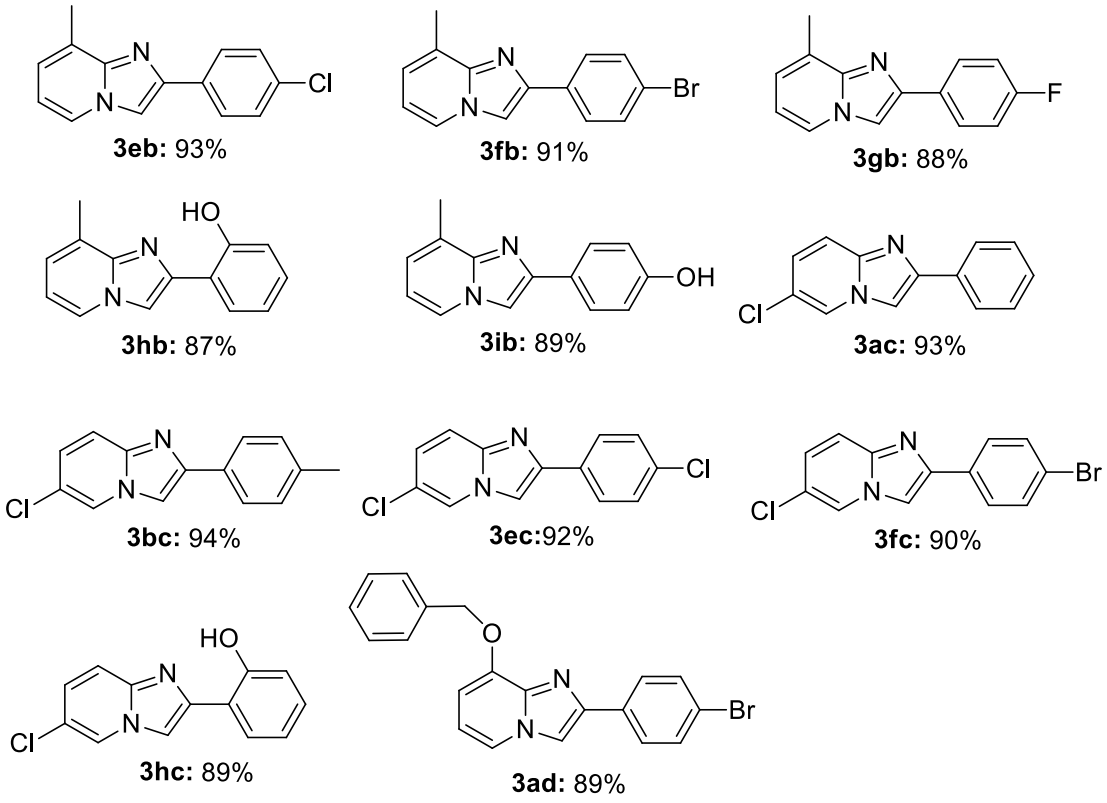
3ab: 91%



3cb:88%



3db:92%

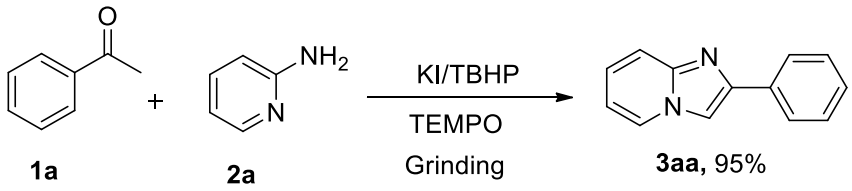


[a] **Reaction Condition:** Acetophenone (1.0 mmol), 2-aminopyridine (1.2 mmol), KI (0.5 equiv.) and oxidizing agent (1 equiv.). [b] Isolated yield.

6-chloro-2-phenylimidazo[1,2-a]pyridine (**3ac**), 6-chloro-2-(p-tolyl)imidazo[1,2-a]pyridine (**3bc**), 6-chloro-2-(4-chlorophenyl)imidazo[1,2-a]pyridine (**3ec**), 2-(4-bromophenyl)-6-chloroimidazo[1,2-a]pyridine (**3fc**), 2-(6-chloroimidazo[1,2-a]pyridin-2-yl)phenol (**3hc**), in good to excellent yield (**Table 4.2**). To our delight 2- aminopyridine containing benzyloxy substituent also gave the corresponding product *viz.* 8-(phenoxymethyl)-2-phenylimidazo[1,2-a]pyridine (**3ad**) in good yield. These results show that these nucleophiles did not affect the proficiency of the reaction (**Table 4.2**).

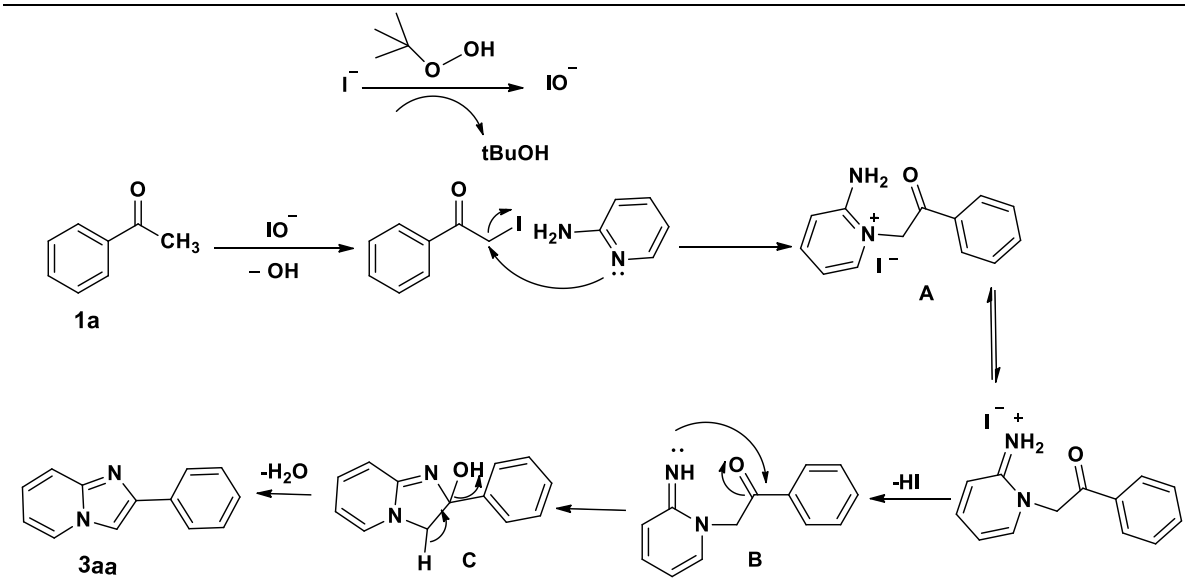
4.3 Plausible Reaction Mechanism

A control experiment has been conducted to explore the reaction mechanism (**Scheme 4.2**). The reaction was performed with radical scavenger TEMPO (2,2,6,6-tetramethylpiperidin-1-yl)oxyl) under optimized condition but it did not quench the reaction. It rules out the possibility of radical pathway of the reaction.



Scheme 4.2: Control experiment with TEMPO.

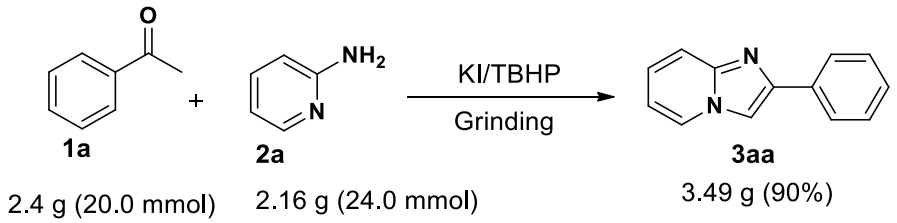
On the basis of literature reports and our observations, a plausible mechanism has been shown in **Scheme 4.3**. First, iodide is oxidized to hypoiodite by TBHP followed by the formation of iodoketone. This iodoketone produced the pyridinium salt (**A**) by the reaction of pyridyl nitrogen with the α-carbon of iodoketone. **A** undergoes deprotonation to give imine **B** which convert into tetrahydroimidazo[1,2-a]pyridin-2-ol (**C**) by intramolecular cyclization. Intermediate **C** then gives the final product, imidazo [1,2-a]pyridine (**3aa**) by the elimination of water.



Scheme 4.3: Plausible reaction mechanism.

4.4 Scalability of the Protocol

After developing this methodology, gram scalability have been demonstrated for this method. The reaction was performed with acetophenone (**1a**) **(**2.4 g, 20.0 mmol), 2-amino pyridine (**2a**) (2.16 g, 24.0 mmol) under optimized reaction conditions and it gave 90% (3.49 g) yield of the product (**3aa**) which is similar to the mmol scale synthesis. This indicates that our methodology is also effective for gram scale synthesis (**Scheme 4.4**).



Scheme 4.4: Gram scale synthesis of imidazo [1,2-a]pyridine.

4.5 Experimental Section

4.5.1 General procedure for the synthesis of products

A mixture of aryl methyl ketone (1.0 mmol), 2-amino pyridine (1.2 mmol), KI (0.5 equiv.) and TBHP (70% aq., 1 equiv.) were taken in mortar and ground continuously. The progress of the reaction was monitored by TLC. The syrup formed was diluted with ethyl acetate and washed with water. The organic layer was dried over anhydrous sodium sulphate (Na_2SO_4), concentrated and subjected to silica gel (60-120 mesh) column chromatography purification (SiO_2: ethyl acetate/hexane) to obtain the pure desired products.

4.5.2 Procedure for gram scale synthesis

A mixture of acetophenone (20.0 mmol), 2-amino pyridine (24.0 mmol), KI (0.5 equiv.) and TBHP (70% aq., 1 equiv.) were added in mortar and ground continuously and the progress of the reaction was monitored by TLC. The obtained syrupy was diluted with ethyl acetate and washed with water. The organic layer was dried over anhydrous sodium sulphate (Na_2SO_4), concentrated and subjected to silica gel (60-120 mesh) column chromatography purification (SiO_2: ethyl acetate/hexane) to obtain the pure desired products in 90% yield.

4.5.3 Procedure for control experiment with TEMPO

Acetophenone (**1a**) (1.0 mmol), 2-amino pyridine (**2a**) (1.2 mmol), KI (0.5 equiv.), TBHP (70% aq., 1 equiv.) and TEMPO (1.0 mmol) were taken in mortar and ground

continuously. Progress of the reaction was monitored by TLC. The formed syrup was diluted with ethyl acetate and washed with water. The organic layer was dried over anhydrous sodium sulphate (Na_2SO_4), concentrated and subjected to silica gel (60-120 mesh) column chromatography purification (SiO_2:ethyl acetate/hexane) to obtain the pure desired product.

4.6 Analytical Data

4.6.1 2-Phenylimidazo[1,2-a]pyridine (3aa): White crystalline solid; yield 184 mg (95%); m.p. 135-136 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.11 (dt, 1H), 7.99 – 7.93 (m, 2H), 7.86 (s, 1H), 7.63 (dd, 1H), 7.48 – 7.39 (m, 2H), 7.37 – 7.29 (m, 1H), 7.20 – 7.13 (m, 1H), 6.77 (td, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 145.9, 145.8, 133.9, 128.8, 128.1, 126.1, 125.7, 124.7, 117.7, 112.5, 108.2.

4.6.2 2-(p-Tolyl)imidazo[1,2-a]pyridine (3ba): White solid; yield 193 mg (93%); m.p. 143-144 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.38 (d, 1H), 7.84 (d, 2H), 7.78 (s, 1H), 7.44 (d, 1H), 7.34 (dd, 1H), 7.27 (d, 2H), 2.41 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 146.5, 144.2, 138.3, 132.5, 130.5, 130.4, 129.6, 126.1, 118.5, 107.5, 21.4.

4.6.3 2-(4-Methoxyphenyl)imidazo[1,2-a]pyridine (3ca): White solid; yield 210 mg (94%); m.p. 138-139 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.09 (dd, 1H), 7.88 (d, 2H), 7.77 (s, 1H), 7.61 (d, 1H), 7.18 – 7.13 (m, 1H), 6.97 (d, 2H), 6.75 (t, 1H), 3.85 (s, 3H); **^{13}C**

NMR (126 MHz, CDCl3) δ (ppm): 159.7, 145.8, 145.7, 127.4, 126.5, 125.5, 124.6, 117.4, 114.2, 112.4, 107.3, 55.4.

4.6.4 2-(3-Nitrophenyl)imidazo[1,2-a]pyridine (3da): Yellow solid; yield 227 mg (95%); m.p. 202-203 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.77 – 8.74 (m, 1H), 8.32 (d, 1H), 8.17 (dd, 2H), 7.98 (s, 1H), 7.65 (d, 1H), 7.60 (t, 1H), 7.23 (d, 1H), 6.84 (t, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 148.8, 146.0, 143.5, 135.8, 131.9, 129.8, 125.9, 125.5, 122.6, 120.9, 117.9, 113.1, 109.1.

4.6.5 2-(4-Chlorophenyl)imidazo[1,2-a]pyridine (3ea): Yellow solid; yield 211 mg (92%); m.p. 206-207 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.11 (d, 1H), 7.89 (d, 2H), 7.84 (s, 1H), 7.62 (d, 1H), 7.40 (d, 2H), 7.18 (dd, 1H), 6.79 (t, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 145.8, 144.8, 133.8, 132.4, 129.0, 127.4, 125.7, 125.0, 117.7, 112.7, 108.3.

4.6.6 2-(4-Bromophenyl)imidazo[1,2-a]pyridine (3fa): Off white solid; yield 246 mg (90%); m.p. 200-201 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.10 (dt, 1H), 7.85 – 7.78 (m, 3H), 7.61 (d, 1H), 7.57 – 7.49 (m, 2H), 7.20 – 7.12 (m, 1H), 6.78 (td, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 145.8, 144.8, 132.9, 131.9, 127.6, 125.7, 125.0, 122.0, 117.7, 112.7, 108.3.

4.6.7 2-(4-Fluorophenyl)imidazo[1,2-a]pyridine (3ga): Pale yellow solid; yield 199 mg (94%); m.p. 164-165 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.11 (d, 1H), 7.95 – 7.90 (m, 2H), 7.80 (s, 1H), 7.62 (d, 1H), 7.17 (t, 1H), 7.14 – 7.09 (m, 2H), 6.78 (t, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 163.8, 161.8, 145.8, 145.1, 130.1, 130.1, 127.8, 127.8, 125.7, 124.9, 117.6, 115.8, 115.7, 112.6, 107.9.

4.6.8 2-(Imidazo[1,2-a]pyridin-2-yl)phenol (3ha): Colourless solid; yield 187 mg (89%); m.p. 200-201 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 12.72 (s, 1H), 8.16 (d, 1H), 7.87 (s, 1H), 7.60 (d, 2H), 7.23 (t, 2H), 7.04 (dd, 1H), 6.93 – 6.82 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 157.4, 145.5, 143.6, 129.8, 125.8, 125.5, 125.2, 119.1, 117.8, 116.9, 116.3, 113.2, 106.8.

4.6.9 4-(Imidazo[1,2-a]pyridin-2-yl)phenol (3ia): Brown solid; yield 185 mg (88%); m.p. 230-231 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 9.62 (s, 1H), 8.47 (d, 1H), 8.20 (s, 1H), 7.78 (d, 2H), 7.53 (d, 1H), 7.22 – 7.17 (m, 1H), 6.85 (d, 2H), 6.83 (s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 157.3, 144.6, 127.0, 126.7, 126.6, 124.9, 124.6, 115.5, 115.5, 112.0, 107.6, 107.5.

4.6.10 2-(Pyridin-2-yl)imidazo[1,2-a]pyridine (3ja): Brown solid; yield 166 mg (85%); m.p. 240-241 °C; **^{1}H NMR** (500 MHz, DMSO) δ (ppm): 8.61 – 8.55 (m, 2H), 8.48 (s, 1H), 8.11 (dd, 1H), 7.87 (d, 1H), 7.60 (d, 1H), 7.34 – 7.27 (m, 2H), 6.92 (d, 1H); **^{13}C NMR** (126

MHz, DMSO) δ (ppm): 152.8, 149.5, 147.6, 144.9, 144.6, 137.0, 127.3, 125.4, 122.8, 119.8, 116.9, 112.6, 111.4, 108.0.

4.6.11 2-(Thiophen-2-yl)imidazo[1,2-a]pyridine (3ka): Yellowish white solid; yield 184 mg (92%); m.p. 135-136 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.07 (d, 1H), 7.76 (s, 1H), 7.60 (d, 1H), 7.49 – 7.45 (m, 1H), 7.32 – 7.28 (m, 1H), 7.18 – 7.13 (m, 1H), 7.11 – 7.07 (m, 1H), 6.76 (t, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 145.63, 141.06, 137.67, 127.88, 125.56, 125.20, 124.96, 123.86, 117.53, 112.71, 107.58.

4.6.12 2-(Naphthalen-1-yl)imidazo[1,2-a]pyridine (3la): Yellowish liquid; yield 227 mg (93%); **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.63 – 8.56 (m, 1H), 8.17 (d, 1H), 7.92 – 7.87 (m, 2H), 7.83 (d, 2H), 7.71 (d, 1H), 7.58 – 7.49 (m, 3H), 7.23 – 7.18 (m, 1H), 6.82 (s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 145.48, 145.34, 134.08, 131.87, 131.63, 128.59, 128.47, 127.83, 126.55, 126.06, 125.89, 125.66, 125.52, 124.71, 117.85, 112.55, 111.32.

4.6.13 8-Methyl-2-phenylimidazo[1,2-a]pyridine (3ab): Pale yellow solid; yield 189 mg (91%); m.p. 119-120 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.00 (t, 1H), 7.98 (d, 2H), 7.83 (s, 1H), 7.45 (dd, 2H), 7.37 – 7.31 (m, 1H), 6.96 (d, 1H), 6.68 (t, 1H), 2.68 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 146.3, 145.3, 134.2, 128.7, 127.8, 126.2, 123.5, 123.3, 112.4, 108.6, 17.2.

4.6.14 2-(4-Methoxyphenyl)-8-methylimidazo[1,2-a]pyridine (3cb): Pale yellow solid; yield 209 mg (88%); m.p. 132-133 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 7.95 (d, 1H), 7.89 (d, 2H), 7.73 (s, 1H), 6.97 (d, 2H), 6.92 (d, 1H), 6.64 (t, 1H), 3.84 (s, 3H), 2.65 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 159.5, 146.2, 145.2, 127.5, 127.4, 126.9, 123.4, 123.2, 114.1, 112.2, 107.8. 55.4, 17.2.

4.6.15 8-Methyl-2-(3-nitrophenyl)imidazo[1,2-a]pyridine (3db): Yellow solid; yield 233 mg (92%); m.p. 168-169 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.79 – 8.73 (m, 1H), 8.31 (dd, 1H), 8.16 – 8.11 (m, 1H), 8.00 (d, 1H), 7.92 (s, 1H), 7.57 (t, 1H), 6.98 (dd, 1H), 6.71 (t, 1H), 2.65 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 148.7, 146.5, 142.8, 136.1, 132.0, 129.6, 128.0, 124.0, 123.7, 122.3, 120.9, 113.0, 109.5, 17.1.

4.6.16 2-(4-Chlorophenyl)-8-methylimidazo[1,2-a]pyridine (3eb): White solid; yield 226 mg (93%); m.p. 119-120 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 7.98 (d, 1H), 7.90 (d, 2H), 7.81 (s, 1H), 7.39 (d, 2H), 6.96 (d, 1H), 6.69 (t, 1H), 2.65 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 146.4, 144.2, 133.5, 132.8, 128.9, 127.7, 127.5, 123.6, 123.5, 112.6, 108.7, 17.2.

4.6.17 2-(4-Bromophenyl)-8-methylimidazo[1,2-a]pyridine (3fb): Yellow solid; yield 261 mg (91%); m.p. 131-132°C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 7.97 (d, 1H), 7.87 – 7.82 (m, 2H), 7.79 (s, 1H), 7.55 (d, 2H), 6.96 (d, 1H), 6.71 – 6.64 (m, 1H), 2.65 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 146.4, 144.2, 133.2, 131.8, 123.6, 123.5, 121.7, 112.6, 108.8, 17.2

4.6.18. 2-(4-Fluorophenyl)-8-methylimidazo[1,2-a]pyridine (3gb): White solid; yield 199 mg (88%); m.p. 128-129 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 7.96 (s, 1H), 7.93 (dd, 2H), 7.77 (s, 1H), 7.16 – 7.07 (m, 2H), 6.98 – 6.92 (m, 1H), 6.67 (t, 1H), 2.65 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 163.7, 161.8, 146.3, 144.5, 130.5, 130.4, 127.9, 127.9, 127.7, 123.5, 115.78, 115.6, 112.5, 108.3, 77.4, 77.1, 76.9, 17.1.

4.6.19 2-(8-Methylimidazo[1,2-a]pyridin-2-yl)phenol (3hb): White solid; yield 195 mg (87%); **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 12.94 (s, 1H), 8.00 (s, 1H), 7.83 (dd, 1H), 7.58 (d, 1H), 7.26 – 7.19 (m, 1H), 7.06 – 6.98 (m, 2H), 6.88 (t, 1H), 6.76 (d, 1H), 2.59 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 157.4, 144.7, 144.0, 129.6, 126.8, 125.7, 124.1, 123.2, 119.0, 117.7, 116.4, 113.3, 107.2, 16.9.

4.6.20 4-(8-Methylimidazo[1,2-a]pyridin-2-yl)phenol (3ib): Brown solid; yield 199 mg (89%); **^{1}H NMR** (500 MHz, DMSO) δ (ppm): 10.50 (s, 1H), 9.56 (s, 1H), 8.32 (dd, 2H), 8.26 (s, 1H), 8.18 (s, 1H), 7.80 – 7.75 (m, 3H), 6.99 – 6.95 (m, 1H), 6.84 (d, 1H), 6.77 – 6.75 (m, 1H), 2.51 (s, 3H); **^{13}C NMR** (126 MHz, DMSO) δ (ppm): 157.6, 156.7, 145.6, 145.5, 144.7, 143.0, 136.2, 127.7, 127.4, 126.2, 125.5, 124.8, 123.4, 115.9, 112.3, 109.0, 108.4, 17.1.

4.6.21 6-Chloro-2-phenylimidazo[1,2-a]pyridine (3ac): White solid; yield 213 mg (93%); m.p. 207-208 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.17 (d, 1H), 7.94 (d, 2H), 7.84 (s, 1H), 7.58 (d, 1H), 7.44 (t, 2H), 7.36 (d, 1H), 7.14 (dd, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 147.0, 144.2, 133.4, 128.9, 128.4, 126.2, 126.1, 123.5, 120.7, 118.0, 108.6.

4.6.22 6-Chloro-2-(p-tolyl)imidazo[1,2-a]pyridine (3bc): Pale yellow solid; yield 228 mg (94%); m.p. 125-126 °C; **^{1}H NMR** (500 MHz, CDCl3) δ (ppm): 8.13 (d, 1H), 7.81 (d, 2H), 7.77 (s, 1H), 7.56 (d, 1H), 7.24 (d, 2H), 7.12 (d, 1H), 2.39 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 147.0, 144.1, 138.3, 130.5, 129.6, 126.0, 126.0, 123.4, 120.5, 117.8, 108.2, 21.4.

4.6.23 6-Chloro-2-(4-chlorophenyl)imidazo[1,2-a]pyridine (3ec): Pale yellow solid; yield 242 mg (92%); m.p. 206-207 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.16 (d, 1H), 7.86 (d, 2H), 7.80 (s, 1H), 7.56 (d, 1H), 7.40 (d, 2H), 7.15 (dd, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 145.9, 144.2, 134.2, 131.9, 129.1, 127.4, 126.4, 123.5, 120.9, 118.0, 108.6.

4.6.24 2-(4-Bromophenyl)-6-chloroimidazo[1,2-a]pyridine (3fc): Yellow solid; yield 277 mg (90%); m.p. 199-200 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.15 (dd, 1H), 7.81 – 7.78 (m, 3H), 7.56 (d, 3H), 7.15 (dd, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 145.9, 144.2, 132.4, 132.0, 127.7, 126.5, 123.5, 122.4, 120.9, 118.0, 108.6.

4.6.25 2-(6-Chloroimidazo[1,2-a]pyridin-2-yl)phenol (3hc): White solid; yield 218 mg (89%); m.p. 197-199 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.24 (d, 1H), 7.87 (s, 1H), 7.61 – 7.56 (m, 2H), 7.25 (ddd, 2H), 7.06 (d, 1H), 6.92 (t, 1H), 6.68 (t, 1H), 1.27 (s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 157.4, 146.5, 142.0, 130.1, 127.1, 126.6, 125.9, 123.3, 120.8, 119.2, 117.9, 117.2, 115.8, 107.2.

4.6.26 8-(Phenoxymethyl)-2-phenylimidazo[1,2-a]pyridine (3ad): Pale yellow solid; yield 337 mg (89%); m.p. 130-131 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 7.89 – 7.85 (m, 2H), 7.80 (s, 1H), 7.72 (dd, 1H), 7.55 – 7.49 (m, 4H), 7.38 (dd, 2H), 7.33 (d, 1H), 6.59 (dd, 1H), 6.45 (d, 1H), 5.39 (s, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm): 148.0, 144.0, 140.5, 136.3, 132.86, 131.8, 128.7, 128.2, 127.8, 127.3, 121.8, 118.8, 112.5, 109.3, 103.4, 70.98.

4.7 Spectral Data of Synthesized Product

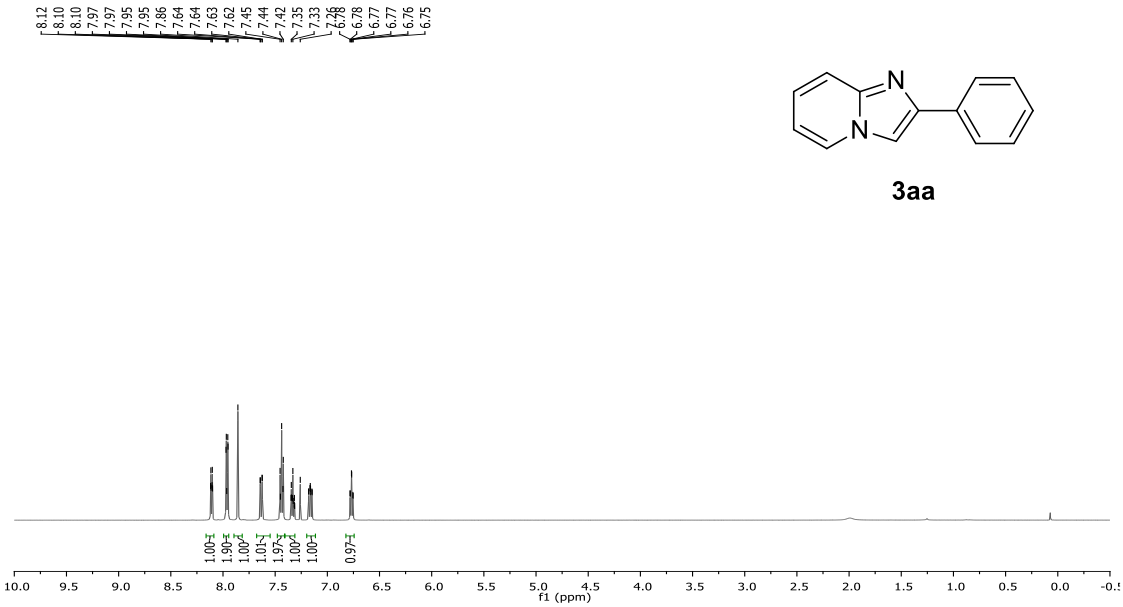


Figure 4.2: ^{1}H NMR of model compound **3aa**.

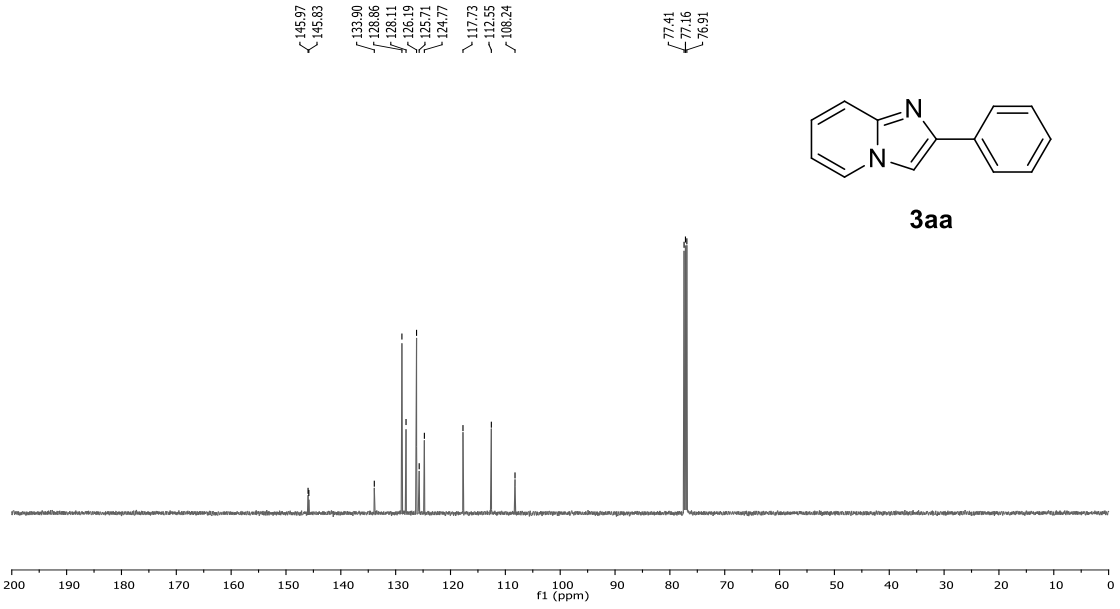


Figure 4.3: ^{13}C NMR of model compound **3aa**.

4.8 Reference

Abe, Y., H. Kayakiri, S. Satoh, T. Inoue, Y. Sawada, K. Imai and N. Inamura, "A novel class of orally active non-peptide bradykinin B2 receptor antagonists 1. Construction of the basic framework,"*Journal of medicinal chemistry*, **41**(4) (1998) 564-578.

Almirante, L., L. Polo, A. Mugnaini, E. Provinciali, P. Rugarli, A. Biancotti, A. Gamba and W. Murmann, "Derivatives of imidazole. I. Synthesis and reactions of imidazo[1,2-α] pyridines with analgesic, antiinflammatory, antipyretic, and anticonvulsant activity," *Journal of medicinal chemistry*, **8**(3) (1965) 305-312.

Ando, K. and K. Yamada, "Highly E-selective solvent-free Horner–Wadsworth–Emmons reaction catalyzed by DBU," *Green Chemistry*, **13**(5) (2011) 1143-1146.

Bhagat, S. B. and V. N. Telvekar, "NBS mediated protocol for the synthesis of N-bridged fused heterocycles in water," *Tetrahedron Letters*, **58**(37) (2017) 3662-3666.

Boggs, S., V. I. Elitzin, K. Gudmundsson, M. T. Martin and M. J. Sharp, "Kilogram-scale synthesis of the CXCR4 antagonist GSK812397,"*Organic Process Research & Development*, **13**(4) (2009) 781-785.

Bose, A. K., S. Pednekar, S. N. Ganguly, G. Chakraborty and M. S. Manhas, "A simplified green chemistry approach to the Biginelli reaction using Grindstone Chemistry," *Tetrahedron letters*, **45**(45) (2004) 8351-8353.

Byth, K. F., J. D. Culshaw, S. Green, S. E. Oakes and A. P. Thomas, "Imidazo [1,2-a] pyridines. Part 2: SAR and optimisation of a potent and selective class of cyclin-dependent kinase inhibitors," *Bioorganic & medicinal chemistry letters*, **14**(9) (2004) 2245-2248.

Cao, H., H. Zhan, Y. Lin, X. Lin, Z. Du and H. Jiang, "Direct arylation of imidazo[1,2-a] pyridine at C-3 with aryl iodides, bromides, and triflates via copper (I)-catalyzed C–H bond functionalization," *Organic letters*, **14**(7) (2012) 1688-1691.

Chen K. and P. S. Baran, "Total synthesis of eudesmane terpenes by site-selective C–H oxidations," *Nature*, **459** (7248) (2009) 824.

Chernyak, N. and V. Gevorgyan, "General and Efficient Copper-Catalyzed Three-Component Coupling Reaction towards Imidazoheterocycles: One-Pot Synthesis of Alpidem and Zolpidem," *Angewandte Chemie International Edition*, **49**(15) (2010) 2743-2746.

Dangel, B. D., K. Godula, S. W. Youn, B. Sezen and D. Sames, "C− C Bond Formation via C−H Bond Activation: Synthesis of the Core of Teleocidin B4," *Journal of the American Chemical Society*, **124**(40) (2002) 11856-11857.

Elhakmaoui, A., A. Gueiffier, J.-C. Milhavet, Y. Blache, J.-P. Chapat, O. Chavignon, J.-C. Teulade, R. Snoeck, G. Andrei and E. D. Clercq, "Synthesis and antiviral activity of 3-substituted imidazo[1,2-a]pyridines," *Bioorganic & medicinal chemistry letters*, **4**(16) (1994) 1937-1940.

Friscic, T. and W. Jones, "Recent advances in understanding the mechanism of cocrystal formation via grinding," *Crystal Growth and Design*, **9**(3) (2009) 1621-1637.

Ge, W., X. Zhu and Y. Wei, "Aerobic Multicomponent Tandem Synthesis of 3-Sulfenyl imidazo[1,2-a]pyridines from Ketones, 2-Aminopyridines and Disulfides," *European Journal of Organic Chemistry*, **2013**(27) (2013) 6015-6020.

Hamdouchi, C., J. D. Blas, M. D. Prado, J. Gruber, B. A. Heinz and L. Vance, "2-Amino-3-substituted-6-[(E)-1-phenyl-2-(N-methylcarbamoyl) vinyl] imidazo[1,2-a]pyridines as a novel class of inhibitors of human rhinovirus: stereospecific synthesis and antiviral activity," *Journal of medicinal chemistry*, **42**(1) (1999) 50-59.

He, C., J. Hao, H. Xu, Y. Mo, H. Liu, J. Han and A. Lei, "Heteroaromatic imidazo [1,2-a] pyridines synthesis from C–H/N–H oxidative cross-coupling/cyclization," *Chemical Communications*, **48**(90) (2012) 11073-11075.

He, C., J. Hao, H. Xu, Y. Mo, H. Liu, J. Han and A. Lei, "Heteroaromatic imidazo[1,2-a] pyridines synthesis from C–H/N–H oxidative cross-coupling/cyclization," *Chemical Communications*, **48**(90) (2012) 11073-11075.

Huang, H.-M., F. Huang, Y.-J. Li, J.-H. Jia, Q. Ye, L. Han and J.-R. Gao, "A general, simple and green process to access pyrrolo[2,1-a]isoquinolines using a KI/TBHP catalytic system," *RSC Advances*, **4**(52) (2014) 27250-27258.

Humphries, A. C., E. Gancia, M. T. Gilligan, S. Goodacre, D. Hallett, K. J. Merchant and S. R. Thomas, "8-Fluoroimidazo[1,2-a]pyridine: synthesis, physicochemical properties and evaluation as a bioisosteric replacement for imidazo[1,2-a]pyrimidine in an allosteric modulator ligand of the GABAA receptor," *Bioorganic & medicinal chemistry letters*, **16**(6) (2006)1518-1522.

Jain, A. N., "Ligand-based structural hypotheses for virtual screening," *Journal of medicinal chemistry*, **47**(4) (2004) 947-961.

Khan, A. T., R. S. Basha and M. Lal, "Bromodimethylsulfonium bromide (BDMS) catalyzed synthesis of imidazo[1,2-a]pyridine derivatives and their fluorescence properties," *Tetrahedron Letters*, **53**(17) (2012) 2211-2217.

Lacerda, R. B., C. K. F. D. Lima, L. L. D. Silva, N. C. Romeiro, A. L .P. Miranda, E. J. Barreiro and C. A. M. Fraga, "Discovery of novel analgesic and anti-inflammatory 3-arylamine-imidazo[1,2-a]pyridine symbiotic prototypes," *Bioorganic & medicinal chemistry*, **17**(1) (2009)74-84.

Li, H.-L., Y. Wang, P.-P. Sun, X. Luo, Z. Shen and W.-P. Deng, "α, β-Double Electrophilic Addition of Allene-1, 3-Dicarboxylic Esters for the Construction of Polysubstituted Furans by KI/*tert*-Butyl Hydroperoxide (TBHP)-Promoted Oxidative Annulation," *Chemistry–A European Journal*, **22**(27) (2016) 9348-9355.

Li, X., X. Xu, P. Hu, X. Xiao and C. Zhou,"Synthesis of sulfonated oxindoles by potassium iodide catalyzed arylsulfonylation of activated alkenes with sulfonylhydrazides in water," *The Journal of organic chemistry*, **78**(14) (2013) 7343-7348.

Liu, P., C.-L. Deng, X. Lei and G.-Q. Lin, "Tandem Amination/Cycloisomerization of Aryl Propargylic Alcohols with 2-Aminopyridines as an Expedient Route to Imidazo[1,2-a] pyridines," *European Journal of Organic Chemistry*,**2011**(36) (2011) 7308-7316.

Lyon, M. A. and T. S. Kercher, "Glyoxylic acid and MP-glyoxylate: efficient formaldehyde equivalents in the 3-CC of 2-aminoazines, aldehydes, and isonitriles," *Organic letters*, **6**(26) (2004) 4989-4992.

Maheswari, C. U., G. S. Kumar and M. Venkateshwar, "Transition metal and base free synthesis of 2-aryl-2-oxazolines from aldehydes and β-amino alcohols catalysed by potassium iodide," *RSC Advances*, **4**(75) (2014) 39897-39900.

Masquelin, T., H. Bui, B. Brickley, G. Stephenson, J. Schwerkoske and C. Hulme, "Sequential Ugi/Strecker reactions via microwave assisted organic synthesis: novel 3-center-4-component and 3-center-5-component multi-component reactions," *Tetrahedron letters*, **47** (17) (2006) 2989-2991.

Meng, X., C. Yu, G. Chen and P. Zhao, "Heterogeneous biomimetic aerobic synthesis of 3-iodo imidazo[1,2-a]pyridines via CuOx/OMS-2-catalyzed tandem cyclization/iodination and their late-stage functionalization," *Catalysis Science & Technology*, **5**(1) (2015) 372-379.

Mizushige, K., T. Ueda, K. Yukiiri and H. Suzuki, "Olprinone: a phosphodiesterase III inhibitor with positive inotropic and vasodilator effects," *Cardiovascular drug* reviews, **20** (3) (2002) 163-174.

Nada, M. H., E. G. Gillan and S. C. Larsen, "Mechanochemical reaction pathways in solvent-free synthesis of ZSM-5," *Microporous and Mesoporous Materials*, **276**(2019) 23-28.

Palani, T., K. Park, M. R. Kumar, H. M. Jung and S. Lee, "Copper-Catalyzed Decarboxylative Three-Component Reactions for the Synthesis of Imidazo[1,2-a] pyridines," *European Journal of Organic Chemistry*, **2012**(26) (2012) 5038-5047.

Pericherla, K., P. Kaswan, P. Khedar, B. Khungar, K. Parang and A. Kumar, "Copper catalyzed tandem oxidative C–H amination/cyclizations: Direct access to imidazo[1,2-a] pyridines," *RSC Advances*, **3**(41) (2013) 18923-18930.

Reddy, K. R., M. Venkateshwar, C. U. Maheswari and P. S. Kumar,"Mild and efficient oxy-iodination of alkynes and phenols with potassium iodide and *tert*-butyl hydroperoxide," *Tetrahedron Letters*, **51**(16) (2010) 2170-2173.

Rupert, K. C., J. R. Henry, J. H. Dodd, S. A. Wadsworth, D. E. Cavender, G. C. Olini, B. Fahmy and J. J. Siekierka, "Imidazopyrimidines, potent inhibitors of p38 MAP kinase," *Bioorganic & medicinal chemistry letters*, **13**(3) (2003) 347-350.

Santra, S., A. K. Bagdi, A. Majee and A. Hajra, "Iron (III)-Catalyzed Cascade Reaction between Nitroolefins and 2-Aminopyridines: Synthesis of Imidazo[1,2-a]pyridines and Easy Access towards Zolimidine," *Advanced Synthesis & Catalysis,* **355**(6) (2013) 1065-1070.

Starrett, J., E. John, A. T. Montzka, A. R. Crosswell and R. L. Cavanagh, "Synthesis and biological activity of 3-substituted imidazo[1,2-a]pyridines as antiulcer agents," *Journal of medicinal chemistry,* **32**(9) (1989) 2204-2210.

Stasyuk, A. J., M. Banasiewicz, M. K. Cyrański and D. T. Gryko, "Imidazo[1,2-a] pyridines susceptible to excited state intramolecular proton transfer: one-pot synthesis via an Ortoleva–King reaction," *The Journal of organic chemistry,* **77**(13) (2012) 5552-5558.

Wanyi, L., B. Ma, H. Zhan, S. Bi and X. Chen, "Synthesis of bis (indolyl) methanes under dry grinding conditions, promoted by a Lewis acid–surfactant–SiO_2-combined nanocatalyst," *Green Chemistry,* **21**(2019) 3542-3546.

Yan, H., S. Yang, X. Gao, K. Zhou, C. Ma, R. Yan and G. Huang, "Iron (II)-catalyzed denitration reaction: Synthesis of 3-methyl-2-arylimidazo[1,2-a]pyridine derivatives from aminopyridines and 2-methylnitroolefins," *Synlett,* **23**(20) (2012) 2961-2964.

Yu, J., C. Zhang, X. Yang and W. Su, "Decarboxylative acylation of N-free indoles enabled by catalytic amount of copper catalysis and liquid-assisted grinding," *Organic & biomolecular chemistry,***17** (2019) 4446-4451.

Zhang, J., J. Jiang, Y. Li and X. Wan, "Iodide-Catalyzed Synthesis of *N*-Nitrosamines via C–N Cleavage of Nitromethane" *The Journal of organic chemistry*, **78**(22) (2013) 11366-11372.

Zhu, D. -J., J. -X. Chen, M. -C. Liu, J.- C. Ding and H. -Y. Wu, "Catalyst: and solvent-free synthesis of imidazo[1,2-a]pyridines," *Journal of the Brazilian Chemical Society*, **20**(3) (2009) 482-487.